reason why such a bureau should not, before long, be erected into an independent department, second in its influence and importance to none other. Let us have a Secretary of Public Health, as well as a Secretary of War. The achievement of this great national undertaking, as of every other great and good work among men, can only be effected by time and patience, by rational inquiry, and enlightened perseverance. Until this is accomplished, each state must form a plan for the gathering of its own vital statistics, suited to its own circumstances, and must use for this purpose the means it may possess, and the machinery already in operation."

State Office Building, McAllister and Larkin streets.

ALCOHOL TOLERANCE: ITS IMPORTANCE IN RELATION TO CHEMICAL TESTS FOR DRUNKENNESS*

By Henry W. Newman, M. D. San Francisco

THERE are few subjects of medical research more difficult to approach without prejudice than the problem of alcohol. That the excessive use of alcohol beverages is harmful, both physically and mentally, is undisputed. Among intelligent individuals, at least, the controversy is concerned with what constitutes "excessive" drinking. In our present civilization other factors than the toxic action of the drug on the human organism must be considered, particularly when the drinker is in control of a potentially lethal mechanism such as the modern automobile. It is this aspect of the alcohol problem that is dealt with in this paper.

In the past ten or fifteen years increasing stress has been laid on the chemical diagnosis of drunkenness, notably when suspicion of such exists in traffic accidents. In order to appreciate just what information can be obtained from such tests, and how much weight may be placed upon them as evidence in such cases, it is helpful to review certain aspects of our knowledge of the metabolism of alcohol, and its effect on the nervous system.

ALCOHOL ABSORPTION

Alcohol is rapidly absorbed from the gastrointestinal tract. It is one of the relatively few substances absorbed directly from the stomach, but by far the greatest absorption takes place in the upper portion of the small intestine. The presence of food in the stomach, particularly protein, retards absorption. High concentrations of alcohol are more slowly absorbed than are more dilute beverages.¹ Thus, we should expect a higher blood-alcohol concentration in a subject drinking a given amount of alcohol, as a 10 per cent solution on an empty stomach, than would be achieved by the same subject drinking an equal quantity of alcohol, as straight whisky after a heavy dinner. From this we see that the amount of alcohol imbibed is not in itself a good indication of the degree of intoxication.

ABSORPTION RATE

After absorption, about 95 per cent of the alcohol is metabolized in the body, being burned ultimately to carbon dioxid and water. It thus can serve as a source of energy for the bodily requirements, and is capable of supplying a considerable percentage of the basal metabolic requirements. Approximately 5 per cent is excreted, about equal amounts being eliminated in the urine and the expired air. The remarkable thing about the metabolism of alcohol is that it proceeds at a practically constant rate, irrespective of the amount in the body.2 That is, the same length of time is required to burn an ounce of alcohol in the body whether one ounce or ten ounces have been absorbed; so that if we plot a curve of blood-alcohol concentration after a single dose of alcohol against time, it has the form of a straight line. This is important, for it means that from one blood-alcohol determination taken some time after an accident the blood-alcohol concentration at the time of the accident may be approximated. There is no good explanation why alcohol should behave in this manner. It is well established, however, that at least the first of the chain of events in the combustion of alcohol takes place in the liver, as has been shown by Lundsgaard in perfusion of isolated organs. He found that no alcohol disappeared from the perfusion fluid when muscle, such as a hind-limb preparation, was perfused, but that when liver was perfused the disappearance of alcohol was at a rate somewhat over half that which would be expected in the intact animal, a percentage about what would be expected because of the lessened metabolic activity of the liver under the artificial conditions prevailing in any perfusion set-up. The amount of oxygen consumed was not enough, however, to completely oxidize the alcohol, from which he concluded that the intermediary products of alcohol metabolism probably are further oxidized elsewhere. We have been able to confirm this work.

There are very few ways in which this constant rate of alcohol metabolism may be influenced. Muscular activity, the temperature of the external environment, metabolic stimulants, such as thyroid extract or dinitrophenol, all are without effect. Nor are diuretics or respiratory stimulants effective in removing an appreciable amount of alcohol from the body. Ingested protein or amino-acids do increase the rate of alcohol metabolism by a small amount, and large doses of insulin are capable of causing an increase of over 40 per cent. Apart from these agents, the disappearance of alcohol from the body proceeds at a constant rate, which varies but little from individual to individual of the same species.

CHEMICAL TESTS OF DRUNKENNESS

The chemical tests of drunkenness consist essentially of the determination of the alcoholic content of some body fluid, or of the expired air, and the computation from this figure of the concentration of alcohol in the body. Since there is a practically fixed relationship between the concen-

[•] From the Department of Medicine, Neuropsychiatric Division, Stanford University School of Medicine, San Francisco.

cisco.

Read before a joint meeting of the Section on General
Medicine and Neuropsychiatry of the California Medical
Association at the sixty-eighth annual session, Del Monte,
May 1-4, 1939.

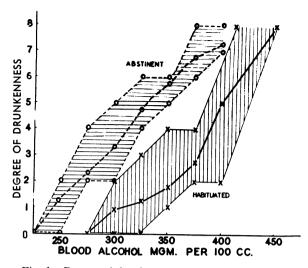
Table 1.—Arbitrary Scale of Degrees of Drunkenness in Dogs

- Slight ataxia on climbing stairs.
 Gross ataxia on climbing stairs.
 Slight ataxia on level; cannot climb stairs.
 Walks briskly, but grossly ataxic.
 Stands and walks one or two steps.
 Makes voluntary movements, but cannot stand.
 No voluntary movements, but lowers head slowly to floor when it is raised.
 Allows head to flop on floor when it is raised.
 Corneal reflex absent.

trations in the various fluids and tissues of the body, as well as in the breath, this is a perfectly valid procedure, and the source of the material for the tests may be chosen solely on the grounds of convenience and freedom from chance contamination. Breath and urine immediately recommend themselves on the basis of availability, and can be collected with a minimum of cooperation on the part of the subject. It has been ruled that breath and urine may be obtained without the consent of the subject, and not be considered as making him testify against himself, much as fingerprints may be used as evidence. This is not true of blood or spinal fluid, which cannot be abstracted without the subject's consent. Because of this disadvantage, as well as the necessity of a trained person for obtaining the specimens, blood and spinal fluid are not practical sources of material for routine alcohol determinations. Breath has the disadvantage of variation in alcohol content with the depth of respiration, and possible chance contamination from belching or the presence of recently imbibed alcohol in the mouth. The latter factor also is to be considered when saliva is used as the source of material for analysis. Thus, it is safe to say that urine is the best material, and breath next in line. The actual analysis is quite simple, and can be performed by any reasonably well-trained technician. Most of the methods depend on the distillation of the alcohol into an oxidizing solution, with the subsequent determination, by titration or colorimetry, of the amount of the oxidant used up, and from this the amount of alcohol in the specimen.⁵ Thus, it is relatively simple and accurate to determine the amount of alcohol in the urine or breath, and from this to calculate the amount present in the blood, not only at the time of securing the specimen, but at the time of the accident, assuming no alcohol has been taken in the interval. Interfering substances are few. Acetone will react as alcohol in the test, but should not be difficult to rule out chemically or clinically, as it is true of ether.

INTOXICATION FROM THE LEGAL STANDPOINT

We have seen that it is not a difficult matter to determine the concentration of alcohol in a subject's blood, and consequently in his brain. However, in order to apply this as evidence of a definite degree of alcoholic intoxication, we must make the assumption that every individual with the same blood-alcohol concentration will show the same degree of drunkenness. Proof of this thesis has been attempted on a large scale, blood-alcohol concentrations being compared with the appraisal of the



Degree of drunkenness in habituated and nonhabituated dogs at various levels of blood alcohol. The shaded areas indicate the range, and the lines the average for each group.

degree of drunkenness on the basis of various tests of performance and by clinical observation. It is true that, considered statistically, there is a high degree of correlation between the two methods; but if we are to give chemical evidence of intoxication by itself a legal standing, it must correlate not only statistically, but invariably. The question actually boils down to this: is there enough individual variation in tolerance to alcohol, whether inherent in the individual or acquired through habituation to the drug, to make invalid the evidence obtained from chemical tests? To answer this question we must know the nature and extent of tolerance to alcohol.

AUTHOR'S STUDIES

It is with this problem that we have been working for the past four years. 6,7,8,9 As it is hardly practicable to test the tolerance of human subjects to alcohol before and after habituation, we chose dogs as our subjects. Accepting as an hypothesis that acquired tolerance did occur, we set out to determine the mechanism which might bring it about. A series of dogs was given a test dose of alcohol first gastrically, and after an interval of a few days, intravenously—to control the factor of absorption. and the blood-alcohol concentration followed at frequent intervals until it fell to zero. We thus had controls on the blood-alcohol concentration following both oral and intravenous administration of alcohol. A period of thirteen months was then allowed to lapse, during which time the animals had as their only supply of fluid a 10 per cent solution of alcohol. They drank, on an average, about seven cubic centimeters of alcohol per kilogram body weight per day, which would be the equivalent of a quart of whisky daily for a man of average weight. At the end of this time the test dose of alcohol was repeated, and the curves of bloodalcohol concentration found to coincide very well with those obtained before habituation. From this data we must conclude that any tolerance developed by the dogs was not due to either decreased absorption or increased rate of metabolism of alcohol.

We then decided to determine if tolerance actually did develop with habituation. To this end, we took a fresh group of animals and subjected them to the test dose of alcohol, and followed not only their blood-alcohol concentration, but also their neuromuscular behavior during the period of intoxication. This we judged in nine degrees, purely arbitrary, as shown in Table 1. As can be seen from Figure 1, there was a certain divergence in the behavior of the individual dogs at the same blood-alcohol levels, indicating some degree of difference in inherent tolerance to alcohol. The period of habituation was then begun. It had previously been noted that the animals, when given free access to the alcohol solution all during the twentyfour hours, soon learned to drink only a little at a time, and so never became very drunk. This we remedied by placing the alcohol solution in the cages for only a short period twice daily, with the result that the dogs became very drunk twice a day, while imbibing almost the same daily dose as the previous group. At the end of ninety-seven days they were subjected to the same procedure after the test dose as before. The rate of alcohol metabolism did not show a significant variation from that shown before habituation, but the degree of drunkenness at a given blood-alcohol level showed a consistent and marked decrease after habituation, as can be seen in Figure 1, in which the heavy line indicates the average degree of drunkenness of the five dogs at the various levels of blood-alcohol, and the shaded area the extent of variation among the different dogs. The lack of overlap of the shaded areas for the abstinent and habituated animals indicates a clear-cut acquired tolerance of all animals. That this tolerance is not permanent was demonstrated by its loss after a period of abstinence of seven months' duration. Thus, we demonstrated that not only do dogs show a variation in tolerance to alcohol from individual to individual, but that this tolerance can be increased by habituation, and again decreases after abstinence. If we can be allowed the privilege of applying these results with dogs to the same problem in man, it is at once apparent that the same blood-alcohol concentration need not indicate the same degree of intoxication in one individual as in another, or even in the same individual should he change his drinking habits.

The importance of these findings in the evaluation of chemical tests for drunkenness is obvious, and makes such, standing alone and without confirmation by clinical observation or performance tests, definitely inconclusive. That the chemical diagnosis of drunkenness is, however, a valuable adjunct to the other tests is equally true.

Department of Medicine.
Stanford University School of Medicine.

REFERENCES

- 1. Mellanby: Medical Research Council, Special Report Series, No. 31, 1919.
- 2. Newman and Cutting: J. Pharm. and Exper. Therap., 54:371, 1935.
- 3. Lundsgaard: Compt. rend. du Lab. Carlsberg, Ser. chim., 22:333, 1937.
 - 4. Newman and Cutting: J. Clin. Invest., 14:945, 1935.

- 5. Newman: J. Pharm. and Exper. Therap., 56:278, 1936
- 6. Newman and Cutting: J. Pharm. and Exper. Therap., 55:82, 1935.
- 7. Newman and Cutting: J. Pharm. and Exper. Therap., 57:388, 1936.
- 8. Newman and Lehman: J. Pharm. and Exper. Therap., 62:301, 1938.
- 9. Newman and Card: J. Pharm. and Exper. Therap., 59:249, 1937.

ALCOHOLISM: ITS PSYCHIATRIC TREATMENT*

By J. L. Henderson, M. D. Compton

ALCOHOL is used by almost all races. Every cultural group has its drink or drinks, the essential ingredient of which is alcohol. History indicates this is also true of the past. The intoxication produced, therefore, must be universally pleasing to the drinker. In general, mild intoxication is socially acceptable. It lessens the critical faculties. Speech flows more freely. Self-assertion comes into the foreground. The world becomes more mellow, companions more jovial-a pleasant letdown after the tension and strain of the day. But if the intoxication deepens, the veneer of civilization becomes thinner, and the primitive forces in the personality begin to appear. The drinker then may become obnoxious, except possibly to others likewise inebriated. To certain persons alcoholic intoxication, instead of a pleasant interlude in an otherwise exacting existence, becomes a narcotic necessary to make such existence tolerable. Such dependence upon drinking results in alcoholism, and constitutes the problem with which we are concerned. The extent of this problem varies in different countries, but seems to be more widespread where the cultural requirements are exacting. Thus, it would seem to be an effect of the progress of civilization, dependent upon the inability of certain persons to meet its requirements. Most alcoholics fear their incapacity to meet the essential conditions expected of them, with secondary rebellion against such conditions and against the persons who demand compliance.

RECENT INCREASE OF ALCOHOLISM

As an indication of the recent increase of alcoholism, the statistics of one life insurance company indicate that, in 1932, 11.9 persons of every one hundred applying for life insurance were rejected because of "heavy alcoholic indulgence." In 1936 this figure had increased to 33.7 of every one hundred such persons, an increase of 183 per cent in four years. The Department of Psychiatry of Bellevue Hospital, New York City, treats one thousand alcoholic patients a month; and the director, Dr. Karl Bowman, points out that temporary treatment by fines and jail sentences does not cure this condition. It is impossible to estimate the enormous economic loss involved. But more im-

^{*} From the Compton Sanitarium.

Read before a joint meeting of the Section on General Medicine and Neuropsychiatry of the California Medical Association at the sixty-eighth annual session, Del Monte, May 1-4, 1939.